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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference<br>BP/G-32575A/SAG/GBG | **FOR FURTHER ACTION** | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| International application No.<br>PCT/EP 03/07349 | International filing date *(day/month/year)*<br>08.07.2003 | Priority date *(day/month/year)*<br>09.07.2002 |
| International Patent Classification (IPC) or both national classification and IPC<br>A61K47/00 | | |
| Applicant<br>SANDOZ AG et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report. |
|---|---|
| 22.12.2003 | 16.11.2004 |
| Name and mailing address of the international preliminary examining authority:<br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized Officer<br>Estañol Y Cornella,<br>Telephone No. +49 89 2399-8647 |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/07349

## I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

**Description, Pages**

1-17 as originally filed

**Claims, Numbers**

1-29 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 1-29 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | 1-29 |
| | No: | Claims | |
| Industrial applicability (IA) | Yes: | Claims | 1-29 |
| | No: | Claims | |

2. Citations and explanations

**see separate sheet**

**Item V.**

Reference is made to the following document:

D1: EP-A-0 955 062 (GENENTECH INC) 10 November 1999 (1999-11-10)

None of the documents of the available prior art discloses a multi-dosage liquid formulation with a concentration of from about 5 mg/ml to about 100 mg/ml human growth hormone (hGH) and 1,2-propylene glycol, a buffer, a non-ionic surfactant and a preservative, having a pH of 6.1 to 6.3. Thus, the subject-matter of claim 1 is new over the available prior art (Art. 33(2) PCT).

The problem underlying the present invention may be regarded as hor to provide alternative storage stable liquid pharmaceutical compositions of high concentrations of hGH.

D1 has solved the same problem by liquid formulations of hGH having a pH of 6.0 and comprising 5mg/ml of hGH, polysorbate or poloxamer as non-ionic surfactant, sodium citrate as buffer and phenol as preservative. The aqueous formulations of D1 are storage stable at 2-8°C for up to one year and at temperatures above 8°C (see page 5, example I).
The difference between D1 and the present invention is that the later further includes 1,2-propylene glycol. None of the documents of the available prior art either discloses or suggested the addition of 1,2-propylene glycol to hGH formulations in order to solve the problem posed.
The subject-matter of present claim 1 involves therefore an inventive step according to Art. 33(3) PCT.

The pH value seems to be essential for carrying the invention and seems to have to be within a narrow range, namely from 6.1 to 6.3. Thus, the term "about" used in claim 1 for defining the pH value is vague and unclear (Art. 6 PCT).